## REMARKS

Claims 7, 20, 21 and 28-58 are pending in the application. By this Amendment, claims 28, 34 and 40 have been amended. Support for this amendment is found at least at claims 1-22 as originally filed.

**It is requested that the Examiner make of record this Amendment After Final since the amendments serve to place the claims in a condition for allowance and raise no new issues for examination.**

The applicants acknowledge the Examiner's withdrawal of the following rejections:

(i) the rejection of claims 20 and 34 under 35 U.S.C. § 102(b) based upon U.S. Patent No. 4,254,129 of Carr *et al.* ("Carr") (Office Action at ¶ 3);

(ii) rejection of claims 30-33, 35, and 37 under 35 U.S.C. § 102(e)/103(a) based upon U.S. Patent No. 6,103,735 of Aslanian *et al.* ("Aslanian") (Office Action at ¶ 6);

(iii) the rejection of claims 30-33, 35 and 37 under 35 U.S.C. § 102(e)/103(a) based upon U.S. Patent No. 6,451,815 of Hwang *et al.* ("Hwang") (Office Action at ¶ 10);

(iv) the rejection of claim 21 under 35 U.S.C. § 103(a) as being obvious over Carr in view of Hwang (Office Action at ¶ 14);

(v) the rejection of claims 28, 29, 38, and 39 under 35 U.S.C. § 103(a) based upon Carr taken in view of Hwang (Office Action at ¶ 15);

(vi) the rejection of claims 35 and 36 under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,267,985 of Chen *et al.* ("Chen") (Office Action at ¶ 16).

As a threshold matter, the applicants confirm that that the phrase "100 μg/ml to 100 mg/ml" as used in, *e.g.*, claim 35, is not a typographical error.

### I. Rejection under 35 U.S.C. § 112, second paragraph - indefiniteness.

The Examiner has rejected claims 7, 20, 21, 28, 29, 34, 38, 39, 44, 45, and 47 under 35 U.S.C. § 112, second paragraph for being indefinite. The Examiner has suggested claim

amendments for claims 34 and 28 that will overcome the rejection. The applicants have corrected the claims and accepted the Examiner's suggestions. Accordingly, it is respectfully submitted that the rejection under 35 U.S.C. § 112, second paragraph, has been overcome and is no longer applicable. Applicants request that the Examiner reconsider and withdraw the rejection.

## II. Rejections under 35 U.S.C. § 102(b) and § 103(a) Based Upon Carr.

At numbered paragraphs 4 and 5 of the Office Action, the Examiner has issued a new rejection of claims 40 and 49 under 35 U.S.C. § 102(b) as being anticipated by Carr. As basis for the rejection, the Examiner states that Carr discloses that fexofenadine can be administered in injectable dosages by solution or suspension of the compound in a physiologically acceptable dilutant with a pharmaceutically acceptable carrier that can be a sterile liquid such as water and oils, with or without the addition of a surfactant and other pharmaceutically acceptable adjuvants.

The Examiner also states that Carr discloses that water, saline, aqueous dextrose and related sugar solutions and glycols such as propylene glycol or polyethylene glycol are preferred liquid carriers for injectible solutions. The Examiner contends that Carr, therefore, discloses aqueous vehicles such as water, propylene glycol or polyethylene glycol. The Examiner also points out that Carr can be administered to the nose, throat, and bronchial tubes and appears to assert that the increased solubility of fexofenadine is inherent in the Carr reference as it is "a function of the carrier or excipient and there is no distinction as to why the excipients or carriers of Carr, which are the one claimed, would not be effective in increasing the solubility of fexofenadine."

At numbered paragraph 17 of the Office Action, the Examiner has issued a new rejection of claims 41-43 under 35 U.S.C. § 103(a) as being unpatentable (obvious) over Carr. The Examiner contends that because Carr discloses the composition and methods of the instant claims, it would have been obvious to one of ordinary skill in the art to modify the amount of excipient utilized and arrive at the present invention as described in claims 41-43.

The applicants respectfully traverse each of the rejections.

As discussed in the applicants' prior response, Carr describes substituted piperidine derivatives including fexofenadine, when the "R" groups have specific substituents. However,

there is no disclosure in Carr of the use of a pharmaceutical excipient that increases the solubility of fexofenadine or its salt in water that is a cyclodextrin or glycofurol. Moreover, there is no discussion or guidance in Carr that would have caused one of skill in the art to seek out alternative excipients that increase the solubility of fexofenadine in water.

The disclosure of Carr does not anticipate the invention of claims 40 and 49. Carr does not teach a pharmaceutical excipient that increases the solubility of fexofenadine or its salt in water that is a cyclodextrin and glycofurol, as is present in the invention described in claims 40 and 49. Accordingly, Carr does not teach each element of the invention; therefore, it does not anticipate the claims under 35 U.S.C. § 102(b).

Moreover, the disclosure of Carr does not render the invention of claims 41-43 obvious, as it does not teach or suggest all elements of the claims, nor does the art provide motivation to a person of ordinary skill in the are to modify Carr to arrive at the present invention. As discussed above, Carr does not teach or suggest use of a pharmaceutical excipient that increases the solubility of fexofenadine or its salt in water that is a cyclodextrin and glycofurol as is recited in claims 41-43. Nor is there present in Carr any motivation to modify Carr to arrive at the invention. Carr places no emphasis on the desirability of increasing the solubility of fexofenadine or its salt in water.

For at least these reasons, it is submitted that the Examiner's rejections of claims 40 and 49 under 35 U.S.C. § 102(b) and of claims 41-43 under 35 U.S.C. § 103(a) based upon Carr are overcome. Reconsideration and withdrawal of the rejections is respectfully requested.

## III. Rejections under 35 U.S.C. § 102(e) and § 103(a) based upon Aslanian.

At paragraphs 7 and 8, the Examiner has rejected claims 40, 41, 49, and 50-57 under 35 U.S.C. § 102(e) as anticipated by Aslanian. The Examiner reasons that Aslanian discloses that water-propylene glycol solutions are suitable for parenteral injections and oral solutions and may contain the drug of interest such as fexofenadine combined with its disclosure that a solution or suspension of the Aslanian composition can be used in the eye, ear or nose renders the claimed invention anticipated.

At paragraph 9, the Examiner has rejected claims 42 and 43 under 35 U.S.C. § 103(a) as being unpatentable over Aslanian. The Examiner contends that Aslanian discloses the composition and methods of the claims as noted above. However, the Examiner concedes that

Aslanian does not specifically disclose the amount of excipient to be utilized. However, the Examiner reasons that where the general conditions of the subject matter are taught and encompass the prior art the difference in amounts of excipients will not support the patentability of the subject matter over the prior art unless there is evidence of criticality. Thus, the Examiner contends it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare and use the formulation of Aslanian containing propylene glycol.

The applicants traverse each of these rejections.

As discussed in the applicants' prior filed response, Aslanian describes pharmaceutical compositions that are useful in the treatment of allergic rhinitis and include a combination of therapeutically effective amounts of one or more neurokinen antagonists, $H_3$ antagonists, and/or $H_1$ antagonists, of which phenofexadine is disclosed as an example. Liquid preparations of the Aslanian composition may contain propylene glycol; however, there is no teaching of use of other excipient components for use in the aqueous solutions or liquid preparations of the Aslanian composition.

Claims 40, 41, 49, and 50-57 are not anticipated by Aslanian for Aslanian does not teach all elements of the invention. In contrast to Aslanian, the present invention is directed to an aqueous composition that includes a pharmaceutical excipient that increases the solubility of the fexofenadine or salt in water that is selected from a cyclodextrin and glycofurol. As such excipients are not taught or suggested in Aslanian, it is submitted that Aslanian does not anticipate the invention under any subpart of 35 U.S.C. § 102.

Moreover, Aslanian does not render obvious the invention of claims 42 and 43. At minimum, Aslanian does not teach or suggest all elements of the invention, as discussed above. Additionally, even if Aslanian taught or suggested all elements of the invention, which it does not, a person of skill in the art would not have been motivated to make the modification and arrive at the present invention. Aslanian does not teach or suggest that other excipients such as those included in the present invention, can be included in Aslanian.

In view of the forgoing, it is submitted that the Examiner's rejections of claims 40, 41, 49, and 50-57 under 35 U.S.C. § 102(e) and of claims 42 and 43 under 35 U.S.C. § 103(a) are overcome. Reconsideration and withdrawal of the rejections is respectfully requested.

## IV. Rejections under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a) based upon Hwang.

The Examiner has maintained the rejection of claims 40, 41, 49 and 57 under 35 U.S.C. § 102(e) as anticipated by Hwang. The Examiner contends that since Hwang discloses a composition containing fexofenadine and propylene glycol, the claimed invention is anticipated.

Additionally, the Examiner has rejected claims 42 and 43 under 35 U.S.C. § 103(a) as being obvious over Hwang. In making the obviousness rejection, the Examiner concedes that Hwang does not specifically disclose how much of the excipient is used. The applicants respectfully traverse the rejection.

Hwang discloses compounds of a specific formula such that when R is a hydrogen atom, the formula is that of fexofenadine. Hwang discloses compositions containing a compound of formula (I) and a p-glycol protein inhibitor in the form of a solution or suspension that may contain adjuvents such as propylene glycol. However, no other pharmaceutical excipients that increase the solubility of fexofenadine in water are taught.

Hwang does not anticipate the invention. The invention recited in claims 40, 41, and 49-57, in contrast to Hwang, include a pharmaceutical excipient that increases the solubility of fexofenadine or its salt in water that is one of a cyclodextrin and glycofurol. Hwang does not teach or suggest that the excipients of Hwang may be a cyclodextrin or a glycofurol. For this reason, the disclosure of Hwang does not anticipate the invention.

Moreover, Hwang does not render the claimed invention obvious. First, for the reasons discussed above, the disclosure of Hwang is missing at least one element of the invention of claims 42 and 43. No teaching or suggestion of this missing element is provided in Hwang. Indeed, a person of ordinary skill would not have been motivated to modify the teachings of Hwang to arrive at the invention as claimed. There is no discussion in Hwang of the necessity or the desirability of increasing the solubility of fexofenadine in water. Indeed, the exemplary compositions provided in Hwang are not liquid compositions at all, but are solid compositions, such as tablets or capsules. Thus, there would be no motivation for a person of ordinary skill in the art to modify Hwang by seeking alternative pharmaceutical excipients that increase the solubility of fexofenadine in water such as cyclodextrin and glycofurol. Moreover, because Hwang is unconcerned with the solubility of fexofenadine, there would have been no reasonable expectation for a person of skill in the art to believe that modifying Hwang by switching the excipient would result in a successful drug delivery composition for fexofenadine.

For at least these reasons, it is respectfully submitted that the § 102(e) and the § 103(a) rejection of claims 40, 41, 49-57 and claims 42 and 43, respectively, are overcome. It is requested that the Examiner reconsider and withdraw the rejections.

## V. Rejections under 35 U.S.C. § 103(a) as Being Unpatentable Over U.S. Patent Application Publication No. 2002/0111495 of Magee *et al.* Considered Alone or Combined with Carr.

At paragraph 18, the Examiner has rejected claims 35-37, 30-33, 41, 46, 52-54, and 58 under 35 U.S.C. § 103(a) as being unpatentable over the disclosure of U.S. Patent Application Publication No. 2002/0111495 of Magee *et al.* ("Magee").

At paragraph 19, the Examiner has rejected claims 7, 20, 21, 28, 29, 34, 38, 39, 40, 44, 45, and 47-51 under 35 U.S.C. § 103(a) as being unpatentable over Magee taken in view of Carr.

The applicants respectfully traverse each of the rejections on the ground that neither of the rejections is proper; Magee is not prior art to the instant application. This application claims priority to Great Britain Application No. 9822170.8, filed October 13, 1998. *See,* Declaration and Power of Attorney. In its present form as a patent application publication, the prior art date of Magee is August 15, 2002, well after the earliest priority date of this application. Additionally, should the Magee patent application issue as a United States patent, its § 102(e) date would be January 31, 2001. This date is also well after the earliest priority date of the application. Magee, therefore, cannot be relied upon as the basis of cannot be relied upon as the basis for a prior art rejections.

The applicants have noted that on the face of the Magee patent application publication is listed two other provisional patent applications, one filed in 1997 and one filed in 1998. However, the applicants submit that on the rules relating to priority claims to U.S. provisional applications, neither of these provisional applications can be claimed as the effective filing date of any patent that issues from the Magee application. At minimum, these documents may be considered to be in the public domain as of the time of the publication of Magee, a date well after the earliest priority date of the application.

Accordingly, for at least these reasons, it is respectfully submitted that the rejections based upon Magee are inapplicable. Their reconsideration and withdrawal is respectfully requested.

## CONCLUSION

In view of the foregoing, it is submitted that claims 7, 20, 21, and 28-58 are distinguished over the cited prior art. Reconsideration, withdrawal of the rejections, and issuance of the claims at the earliest opportunity is respectfully requested.

Respectfully submitted,

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(Date)

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